with severe heart failure (HF) in the COPERNICUS study, of whom 132 had a SBP of 85-95 mm Hg and 264 had a SBP of 96-105 mm Hg at the time of randomization. Following initiation of treatment, SBP increased (CRV>PBO) in the patients with low SBP and fell transiently (CRV>PBO) in the patients with higher SBP. Results (see table):

	All-Cause Mortality		Death or HF Hospitalization	
	1-year PBO rate	Hazard ratio (CRV:PBO)	1-year PBO rate	Hazard ratio (CRV:PBO)
85-95 mm Hg	34%	0.77	61%	0.74
96-105 mm Hg	25%	0.61	43%	0.75
106-115 mm Hg	18%	0.65	37%	0.78
116-125 mm Hg	17%	0.61	40%	0.54
> 125 mm Hg	15%	0.60	32%	0.68

Patients with low baseline SBP were at extremely high risk of a major clinical event, the magnitude of risk decreasing with increasing SBP. However, CRV decreased the risk of death and of death or HF hospitalization in all SBP subgroups, the magnitude of benefit being independent of SBP (interaction P=0.64 and P=0.80 for mortality and for death or HF hospitalization, respectively). The rate of permanent withdrawal decreased with increasing baseline SBP (P=0.0001), similarly for PBO and CRV (interaction P=0.25). Hypotension was reported as an adverse effect more with CRV than PBO overall; this difference was not accentuated in the low SBP subgroups.
Conclusions. These results provide the first evidence that CRV is effective and well tolerated in patients with severe HF and a low SBP.

4:45 p.m.

839-4 The Carvedilol Hibernation Reversible Ischemia Trial: Marker of Success (CHRISTMAS)

John G. Cleland, D. J. Pennell, S. G. Ray, A. J. Coats, A. Lahiri, P. W. Macfarlane, J. Dalle Mule, Z. Vered, G. Murray, for the CHRISTMAS Investigators, *Castle Hill Hospital, Kingston Upon Hill, United Kingdom.*

Background: Improved left ventricular ejection fraction (LVEF) in response to beta-blockers is a consistent finding in dilated cardiomyopathy while it is less consistent in ischaemic heart disease (IHD). This heterogeneous response could be explained by the volume of hibernating myocardium or of scarred myocardium.
Methods: Patients with chronic heart failure (HF) of ischaemic etiology and left ventricular systolic dysfunction (wall motion (WM) index ≤ 1.3 by echocardiography, corresponding to a LVEF ≤ 39%) were enrolled in this international double-blind randomised trial. The primary objective was to determine whether the presence of hibernating myocardium predicted the magnitude of improvement in LVEF in response to carvedilol or placebo. Myocardial status (hibernating or non-hibernating) was assessed by correlating the echocardiographic WM findings to the results of myocardial perfusion imaging (MPI). Hibernation was defined as a regional mismatch between impaired WM with preserved myocardial perfusion by MPI. Baseline LVEF was assessed by radionuclide ventriculography (RNVG). Echocardiographic and nuclear studies were blindly assessed by core laboratories. Hibernators and non-hibernators were stratified into two treatment groups of similar size, randomised to carvedilol or placebo, and titrated up to 25 mg bid. The total duration of the trial was about 6 months.
Results: 305 patients were included in the analysis: 90% males (mean age 62 years), 73% angina-free during daily activity, 60% in NYHA class II, 29% in class III. Mean baseline LVEF was 29 ± 11% (SD). 181 (59%) were classified as hibernators. LVEF was unchanged after 6 months in patients on placebo regardless of myocardial status. Both the hibernating and non-hibernating groups showed significant LVEF improvement with carvedilol. Within the carvedilol group, patients with lower LVEF and larger volumes of hibernating myocardium had a greater LVEF response.
Conclusion: These data suggest that some of the effect of carvedilol on LVEF may be mediated through improvement of hibernating myocardium. Medical therapy may be an important adjunct or alternative to revascularisation for patients with hibernating myocardium.

5:00 p.m.

839-5 Effects of Valsartan on Morbidity and Mortality in Heart Failure Patients Not Receiving ACE Inhibitors

Aldo P. Maggioni, Inder Anand, Sidney O. Gottlieb, Roberto Latini, Gianni Tognoni, Jay N. Cohn, on the behalf of Val-HeFT Investigators, *GISSI Group, Milano, Italy, University of Minnesota Hospital and Clinic, Minneapolis, Minnesota.*

Background: ACE-inhibitors (ACE-i) reduce mortality and morbidity in pts with chronic heart failure (CHF). Nonetheless, nearly 20% of potentially eligible pts may not be prescribed on ACE-i.
Aim: To evaluate the effects of the angiotensin II receptor blocker (ARB) valsartan (V) in the pts randomized in the Val-HeFT trial not receiving ACE-inhibitors.
Methods and Results: Val-HeFT was an international, randomized, double-blind trial testing V vs placebo (P) when added to the prescribed treatment of pts with CHF. The two primary end points were all-cause mortality and morbidity defined as all-cause death, resuscitated sudden death, hospitalization for CHF, or administration of iv inotropes or vasodilators for >= 4h without hospitalization. Of the 5010 pts enrolled in the trial, 366 (9.3%) were not treated with ACE-i at baseline, but 39% were on betablockers. Pts already on treatment with an ARB were excluded. Baseline characteristics and concomitant treatments were comparable in V and P groups not taking ACE-i. Analysis of covariance was performed to assess the effect of V in this subgroup (Table).
Conclusion: Val-HeFT has provided the first placebo-controlled outcome data demonstrating a favorable effect of an ARB on mortality and morbidity in pts with CHF not treated with ACE-i. The improved left ventricular function and reduction in BNP confirm the beneficial effect of V on the progression of CHF. Thus, V can be considered a valid alternative to ACE-i in pts who cannot be treated with these recommended drugs.

	V (n=185)	P (n=181)	p
All-cause deaths %	17.3	27.1	0.02
Morbidity %	24.9	42.5	0.0002
HF Hospitalizations %	27.6	64.6	0.01
EF %	4:66+/-9.19	1.68+/-8.01	0.0004
BNP pg/mL	-53+/-166	64+/-337	0.0004
SBP mmHg	-8.1+/-1.2	-3.2+/-1.2	0.004

5:15 p.m.

839-6 Beneficial Effects of Spironolactone Are Independent of Baseline Aldosterone Levels in Severe Congestive Heart Failure: Results From the RALES Neurohormonal Substudy

Michel F. Rousseau, Annie R. Robert, Jean Marie Ketelslegers, Sylvie A. Ahn, Hubert G. Pouleur, *University of Louvain, Brussels, Belgium.*

Background : Spironolactone (spiro), an aldosterone (aldo) receptor antagonist, is known to improve survival in severe congestive heart failure.
Methods : To determine if this beneficial effect was also present in patients with low baseline aldo plasma levels, aldo plasma concentrations (normal value:<0.4nmol/mL) were measured in 125 patients (mean EF:25%,NYHA III-IV, all treated with ACE-Inibitors), randomly assigned to spiro (n=61) and placebo (n=64) in the RALES Trial.
Results : After 24 months of follow-up, 25% of spiro patients had died versus 42% of placebo patients (p<0.05). Further, when patients were divided according to baseline aldo levels ≥ to median (0.38nmol/mL), the benefit of spiro was present in all patients regardless of baseline values (see table). Indeed, although overall mortality tended to be higher in placebo patients with high baseline values (49%) than those with low baseline values (34%), mortality was also higher in the two placebo groups when compared to patients treated with spiro (RR for placebo vs spiro : 1.76 [0.85-3.93] and 1.58 [0.63-4.13], [95% CI] for high and low baseline values respectively). Given the 95% CI overlap, these RR indicate comparable risk reduction in both spiro groups.
Conclusions : the beneficial effects of spiro on survival are not limited to patients with high circulating aldo levels at baseline, suggesting that tissue concentration might play a key role in the pathophysiology of congestive heart failure.

	Spironolactone		Placebo	
	Death	Alive	Death	Alive
≥0.38	n=8	n=21	n=17	n=18
<0.38	n=7	n=25	n=10	n=19

ORAL CONTRIBUTIONS

845 Hypertrophic Cardiomyopathy Septal Ablation, Athletic Heart, and Doxorubicin Toxicity

Tuesday, March 19, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 257W

8:30 a.m.

845-1 Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy: A New Standard of Care

Nasser M. Lakkis, Jennifer Franklin, Donna Killip, Sherif S. Nagueh, Robert Roberts, William Spencer, III, *Baylor College of Medicine, Houston, Texas, MUSC, Charleston, South Carolina.*

Alcohol septal ablation for hypertrophic obstructive cardiomyopathy has been introduced in the US by our group at Baylor College of Medicine in Nov 1996. The purpose of this abstract is to report on the clinical and echocardiographic long-term outcome of the 219 patients treated at our institution. The mean age was 51+/-15 years, 133 patients were males. The peak CK post ablation rose to 1352+/-915 units. The mean resting gradient decreased from 60 +/-38 mm Hg to 19+/-28 at 6 weeks and continued to decrease at one year to 10+/- 19 mmHg and 5+/-10 mmHg at 3 years. The provoked gradients decreased from 94+/-54 mm Hg to 53+/-65, 42+/-37, and 29+/-36 at 6 weeks, one year and three years. Along with these positive results, the septal thickness decreased from 2.07+/-0.5 cm at baseline to 1.6 +/-0.4, 1.3+/-0.4, and 1.2+/-0.4 cm at 6weeks, one year and three years.
NYHA class symptoms for heart failure decreased from 2.7+/- 0.7 to 0.3+/- at 0.6 at 3 years. Twenty-four patients had a redo procedure within 4 months of the initial ablation for residual gradient, symptoms or both. One patient had a second redo for the same reasons. Ten patients underwent myomectomies for failure of the ablation procedure to relieve their symptoms significantly. Nine out of these ten patients had very small septal arteries that supplied only a limited territory of the hypertrophied septum, as evidenced by the smaller enzyme peak (443+/-354)in these patients. Nine patients died on follow-up. One patinet died after open heart surgery for failed ablation, Two patients had unwit-